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Abstracts

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Acute renal failure due to glomerulonephritis in patients over 60. Interest of renal biopsy. *Y. Tanter, P. Dubot, C. Mousson, E. Justrabo, A. Bonnin, B. Jonon, J. M. Chalopin, G. Rifle, Departments of Nephrology and Pathology. University Hospital, Dijon, France.* Oligoanuric acute renal failure (ARF) is not rare in the elderly. Between 1980 and 1986, we treated 273 patients with ARF. Among them 142 (52%) were over 60 years. Renal biopsies were performed in 40 patients (28%) when we suspected glomerulonephritis (GN) (proteinuria > 2 g/liter, macro- or microscopic hematuria), or systemic disease, or when no etiology was obvious, or when diuresis did not increase at the end of the fourth week. No side effects occurred. In 22 cases (55%) the biopsy only showed acute tubular and interstitial nephritis, including 1 myeloma and 1 secondary oxalosis. In 1 case, we observed amyloid nephropathy. In 17 cases (45%), glomerular lesions were isolated or dominant. They were found in 9 women and 8 men (mean age: 69 ± 4.2 years). In 13 cases we noted extracapillary proliferation (RPGN) associated with mesangial proliferation in 3 patients. This lesion seemed idiopathic in 8 cases and was associated with necrotizing angeitis in 5 cases. Two cases were membranoproliferative GN; one of them was associated with type II cryoglobulinemia. One patient had IgA mesangial GN and another one minimal change GN. In addition to dialysis, despite being elderly patients, specific treatments, according to diagnosis, were used: methylprednisolone pulses (15 mg/kg/day) and corticosteroids (I mg/kg/day), immunosuppressive drugs (cyclophosphamide) and/or plasma exchange. In 9 cases (53%), of them 3 RPGN, renal function improved, and patients were off dialysis with a follow–up of 6 months to 6 years. One patient is still on dialysis after 1 year. Seven other patients died, 5 in the first 2 months (5 RPGN). The treatments were not immediately responsible for death. One died of myocardial infarct during a third relapse of RPGN. The last patient died 18 months after starting hemodialysis. This study emphasizes the need for intensive investigation of ARF whatever the patient's age. Indeed, incidence of GN is at least as high as that in younger patients. RPGN is frequent in this series, as in others, and precise histological diagnosis has permited us to set up treatment that is both specific and efficient.

Treatment of refractory congestive heart failure by continuous peritoneal dialysis. *C. Mousson, Y. Tanter, J. M. Rebibou, P. Morelon, G. Dentan, J. M. Chalopin, G. Rifle, Department of Nephrology and Reanimation, Department of Cardiology, University Hospital, Dijon, France.* Continuous ambulatory peritoneal dialysis (CAPD) was used to remove fluid in refractory congestive heart failure (HF). *Patients and methods.* We included in this study 18 patients (P), 13 men and 5 women (age range 39–77 years, mean 60.2). Primary cardiac disease was: valvular disease 7 P, coronary heart disease 7 P, amyloidosis 2 P, primary dilated cardiopathy 1 P, primary pulmonary hypertension 1 P. All patients had NYHA class IV dyspnea, requiring oxygen and even mechanical ventilation in 3 P. Cardiothoracic ratio (CTR) ranged from 0.53 to 0.80 (mean: 0.62). All patients had pulmonary alveolar edema, ascites and gross edemas. Systolic blood pressure (SBP) ranged from 50 to 90 mm Hg (mean: 72). Left ventricular ejection fraction (LVEF) ranged from 14 to 54% (mean: 32). In all cases, HF was intractable despite treatment with vasodilatators, large doses of furosemide, inotropic agents and fluid intake restriction. Seven of them had previous organic renal failure (ORF); serum creatinine level (SCL) ranged from 200 to 500 μmol/liter during the 3 previous months. Eleven P had normal renal function or functional renal failure (FRF) due to low cardiac output. CAPD was carried out using standard techniques (K^+, 3–5 mmol/liter into dialysate). All patients received i.v. heparin. *Results.* Eight P (44%) died before the end of the third week, 6 had ventricular arrhythmia, 2 had sepsis of urinary tract or digestive origin. Weight loss ranged from 2 to 10 kg (mean: 7). Ten P were still alive 1 month after starting CAPD and 9 of them were discharged. Weight loss ranged from 4 to 41 kg (mean: 14). Mean CTR decreased from 0.61 to 0.55. Surprisingly, no significant improvement of LVEF was observed. Dyspnea improved to class II in 6 P and to class III in 4 P. Mean SBP improvement was 20 mm Hg despite discontinuing inotropic agents. Six of these 10 patients died between 2 to 27 months (mean: 9.5) after starting CAPD. Causes of death were: ventricular arrhythmia, 3 P; undernutrition, 2 P; cardiac arrest at home 24 months after discontinuing CAPD, 1 P. CAPD was stopped in 2 of the 10 patients, who had increased diuresis (normal initial renal function). These 2 P then survived from 4 to 24 months before dying (1 ventricular arrhythmia, 1 cardiac arrest). SBP, CTR, fluid overload, LVEF, ORF were not predictive of survival. However, initial nutritional status, the need for mechanical ventilation, amyloidosis and patients who are more than 70 years old seem to indicate poor prognosis. *Conclusion.* CAPD allows long and good quality survival in some patients whose initial status is very serious. Mortality might be lower if these patients were treated earlier. This trial needs to be continued, particularly in patients awaiting graft.

Lack of antireticulin and antiendomysium antibodies in patients with primary IgA nephropathy associated with IgA antibodies to gliadin. *G. Rostoker, C. Andre, A. Branellec, S. Bourhala, J. Laurent, G. Lagrue. Department of Nephrology and Hematology, Inserm U 139, Hôpital Henri–Mondor, Creteil (94010), France.* The association of circulating IgA antibodies to gliadin (J. Laurent, *Am. J. Nephrol* in press) and the decrease of IgA-containing immune complexes on gluten–free diet (R. Coppo, *Clin Nephrol* 26:77–82, 1986), suggest a possible etiologic role for wheat gliadin in primary IgA nephropathy (GN IgA) and a possible association with a latent coeliac disease (CD). Antireticulin and IgA class antiendomysium antibodies are specific immunological markers for CD and dermatitis herpetiformis associated with CD. Antireticulin antibodies were sought in 16 patients having GN IgA with permanent proteinuria (> 1 g/24 hr) and IgA antibodies to gliadin, whereas anti-endomysium antibodies were sought in 4 of these patients. No patient exhibited these autoantibodies. These results and the normal results of the gut absorption test with radiolabelled EDTA and of the jejunal biopsy performed respectively in 5 and 3 IgA GN patients (personal results, unpublished data) suggest that IgA GN is not associated with latent CD. The relationship between wheat gliadins and IgA GN remains hypothetic and needs further investigation.

Enhanced levels of beta-$_2$-microglobuline (β_2m) in lymphocyte culture supernatants: A marker of lymphocyte activation in idiopathic nephrotic syndromes (INS)? *R. Robeva, A. Branellec, J. M. Heslan, P. Lang, G. Rostoker, M. A. Pech, G. Lagrue, Hôpital Henri Mondor, INSERM U139, Créteil, France.* INS is associated with a disorder of T lymphocyte (L) functions and an enhanced production of a lymphokine, the Vascular Permeability Factor (YPF). But VPF is measured by a biological assay (Ovary's method) which is time consuming and sometimes difficult to interpret. It would be important to have an indirect method for investigating L activation. β_2m is secreted by L and tumor

cells and is considered to be a marker of these cells' activity. However, in autoimmune diseases elevation of β_2m serum levels is less than in lymphoproliferative disorders and cancers. We therefore investigated β_2m levels in L culture supernatant. In 21 active INS, β_2m levels in unstimulated L cultures were significantly increased in comparison with those of 15 controls (median 25.5 ng/ml vs. 15 ng/ml, $P < 0.05$, Mann Whitney test); 9 cases had levels higher than upper limit of normal. In 14 prednisone (P) treated INS, β_2m levels were lower than before treatment (median 13.5 ng/ml, $P < 0.001$) and lower in cases with complete remission than in cases with persistent proteinuria. β_2m levels were also lower in 13 cyclosporine (C) treated INS (median 10.5 ng/ml, $P < 0.01$) and in 10 INS in complete remission, without treatment (median 10.5 ng/ml, $P < 0.05$). In vitro the addition of C (100 ng/ml) inhibited the β_2m elevation observed in INS. The same differences between various groups were observed with Con A stimulated L, with higher β_2m levels. Correlation between β_2m level and VPF activity was not significant ($r = 0.44$, $P < 0.1$), but there were too few cases studied simultaneously. High levels of β_2m in supernatant of L culture from INS are conditioned by enhanced cellular synthesis and inhibited by P or by C. Whether this β_2m hyperproduction is the mere reflection of L activation or plays a pothogenic role in the immune process is still speculative.

Immunological abnormalities in hemodialysis patients affected by a carpal tunnel syndrome (CTS). *K. S. Ang, P. Simon, Y. Y. Cavarle, G. Cam, N. Genetet, M. Catheline, Service de Néphrologie, CH La Beauché Sant-Brieuc, Laboratoire de Biochimie B CHU Pontchaillou et Laboratoire d'Immunogénétique CRTS Rennes, France.* $\beta_2$microglobulin amyloidosis (β_2mA) is a prominent feature of the CTS in uremic patients undergoing long-term hemodialysis (HD). The pathogenesis of B_2mA is still unknown. Impaired cellular immunity which is dependent on the duration of end-stage renal disease, and hemodialysis therapy might be determinant among the factors potentially implicated in the occurrence of β_2mA. Eleven uremic patients, 5 with CTS (Group A) and 6 without (Group B) undergoing HD from 8 to 21 years (mean 12 ± 5 yrs for A and 8.5 ± 1.9 yrs for B, NS) were studied. Control blood samples were obtained from 5 age- and sex-matched healthy volunteers (Group C). The present study investigated the serum levels of IgG, IgM, IgA, the cutaneous tests and the peripheral lymphocyte subsets which were measured using monoclonal antibodies. The changes which occurred during dialysis procedure using cuprophan (CUP) and non-cuprophan (AN69-PAN) membranes were also studied. The following results were observed (A vs. B): (1.) the absolute numbers of OKT3 +, OKT4 + cells were significantly lower in HD patients than controls and in Group A than in Group B; OKT3 (m ± SD/mm^3), 387 ± 253 vs. 744 ± 207, P = 0.03; OKT4, 262 ± 115 vs. 589 ± 297, $P = 0.04$. (2.) At the end of HD, the relative proportion of OKT3 + and OKT4 cells increased with AN69-PAN and decreased with CUP. (3.) In the interdialytic period, serum levels of IgG and IgM were significantly lower in patients with CTS than in controls and HD patients without CTS; IgG (m ± SD/g/liter): 10.2 ± 1.4 vs. 15.4 ± 3.2, $P < 0.01$; IgM: 0.65 ± 0.28 vs. 1.65 ± 0.37, p 0.001. 4) delayed hypersensitivity studied by cutaneous tests showed < 3 positive antigens in 4 of 5 patients with CTS against 1 of 16 patients without CTS. These data suggest the association of severe deficiency of T helper cells with hypogammaglobulinemia and anergy in HD patients affected by β_2m amyloidosis.

Histamine release during hemodialysis. *P. Deteix, G. Betail, A. Tridon, G. Gaillard, A. Marques-Verdier, P. Cluzel, J. P. Wauquier, J. C. Alphonse, J. C. Baguet, Service de Néphrologie, CHU St Jacques, Laboratoire d'Immunologie, Faculté de Médecine, Laboratoire "in vitro" Centre Jean Perrin, Laboratoire d'hématologie CHU St Jacques, Clermont-Ferrand, France.* The biocompatibility of a new cellulosic membrane, Hemophane (HE), was compared to that of a reference membrane Cuprophane (CU), with respect to different biologic parameters, including plasma histamine. Ten chronically-hemodialyzed patients were studied. Each of them was dialyzed on each of the two membranes, in random order. Blood was collected at four times during the dialysis procedure: 0, 10, 20 and 180 minutes. Leukocytosis was measured with Technikon H6000. The C3a-desARG anaphylatoxin and plasma histamine were assayed by RIA. There was a more important increase on C3a with CU than with HE (14-fold and 3-fold predialysis values). There was a transient leukopenia only with CU. Plasma histamine level significantly increased during dialysis with CU (peak level 2.04 ± 1.47 ng/ml), while no change was observed with HE ($P < 0.05$). Likewise, basophils decreased by 53% with Cu and only 20% with HE ($P < 0.01$). Thus, basophil and/or mastocyte activation by the anphylatoxins generated from trigering of the alternative pathways of complement is likely to be responsible for hsitamine release. Histamine could be involved in hypersensitivity reactions observed in some dialyzed patients and the possible release of other mediators of anaphylaxis by basophils and mastocytes deserves further investigation.

Free and total catecholamines in patients with chronic renal failure on hemodialysis. *F. Cogny-Van Weydevelt, J. P. Charmes, G. Lachatre, M. Benzakour, G. Nicot, C. Leroux-Robert, Services de Néphrologie et de Pharmacologie Clinique, Hôpital Universitaire Dupuytren, Limoges, France.* A defect in the autonomic nervous system in dialysis patients is now well accepted. This consists principally of a defect in baroreceptor sensitivity. To evaluate the autonomic nervous system in dialysis patients we measured plasma concentrations of free and total norepinephrine (NE) and epinephrine (E) and total dopamine (DA) using HPLC in 18 patients dialyzed with a cuprophan membrane (11 men, 7 women; mean age: 58.6 years). Before dialysis, plasma concentrations of free NE and E, and more particularly, of total NE, E and DA, are significantly higher than in normal subjects ($P < 0.05$). After dialysis we observed a reduction in total NE, E, and DA plasma concentrations although these remained higher than in normal subjects, and a significant increase in free NE and E plasma concentrations. The persistent increase of these sympathetic nervous system activity markers with, in particular, increased free and therefore active NE and E plasma concentrations after dialysis, could represent an important factor of vascular risk in chronic renal failure patients on hemodialysis by a direct vascular effect and modification of lipid concentrations.

Nephrogenic diabetes insipidus and distal tubular acidosis in meticillin-induced interstitial nephritis. *Ph. Vigeral, A. Kanfer, S. Kenouch, B. Mougenot, F. Blanchet, J. Ph. Méry, Service de Néphrologie and Laboratoire d'Explorations Fonctionnelles, Hôpital Bichat and Laboratoire d'Anatomie et de Cytologie Pathologique, Hôpital Tenon, Paris, France.* Distal tubular abnormalities were demonstrated in two patients in whom meticillin induced interstitial nephritis with renal failure. Some degree of renal insufficiency persisted in both patients after the acute episode. The first patient was explored because of polyuria and metabolic acidosis, 2-1/2 months after onset of nephropathy when plasma creatinine was 240 μmol/liter. Diabetes insipidus (DI) was demonstrated after 12 hours of complete fluid restriction: urinary osmolality (Uosm), 528 mOsm/kg (N > 800 mOsm/kg); urinary volume (V), 1.22 ml/min (N < 0.5 ml/mn); free-water clearance (CH_2O), − 0.93 ml/min (N < − 2 ml/mn). These abnormalities were not corrected after DDAVP injection, and plasma ADH was 16.9 pg/ml (N: 3.6 ± 0.8 pg/ml) showing that DI was nephrogenic. Distal tubular acidosis (DTA) was demonstrated by a bicarbonate loading test showing an abnormally low, urine-blood pCO_2 gradient of 16.7 mm Hg (N > 30 mm Hg). The second patient was explored because of polyuria (4 to 6 l/days) 7 months after onset of nephropathy when plasma creatinine was 213 μmol/liter; there was no metabolic acidosis in this patient. Nephrogenic DI was also demonstrated. After fluid restriction, Uosm was 263 mOsm/kg; V, 1.71 ml/min; CH_2O, + 0.23 ml/min; absence of correction of these abnormalities after DDAVP injection; plasma ADH of 8.2 pg/ml. In conclusion, these data show that meticillin-induced interstitial nephritis may result in persistent nephrogenic DI and DTA.

Correction of dialysis anemia by recombinant erythropoietin. *B. Zins, J. Zingraff, F. Peterlongo, L. Bererhi, C. Naret, H. Kreis, N. Casadevall, B. Varet, J. P. Castaigne, T. Drüeke, Necker and Cochin Hospital, E. Rist Center and CILAG Lab., Paris, France.* Erythropoietin deficiency is one of the major causes contributing to the anemia of chronically uremic patients maintained on long-term hemodialysis. We investigated the effect of thrice weekly intravenous administration of recombinant human erythropoietin (rHuEpo) on the anemia of 11 non-transfusion-dependent, chronic hemodialysis patients with a follow-up of at least two months. rHuEpo was provided by Ortho, Cilag and Amgen laboratories, USA and France. Initial dose was 24 IU/kg body weight. It was increased every two weeks by doubling the

previous dose when hemoglobin (Hb) rise was less than 10%. Hb increased from a mean value of 7.5 ± 1.2 (±SD) to 9.3 ± 1.2 g/dl at two months ($N = 11$, $P < 0.001$). This increase was preceded by a significant rise of reticulocyte count. Only one patient did not respond to therapy. The most recently available mean Hb value achieved by the 10 responders is 10.2 ± 1.7 g/dl (±SD). The only non-responder remained stable at 9.3 g/dl after 11 weeks, although he received the highest dose of rHuEpo (384 IU/kg) administered as yet in this study. None of the 10 patients responded to 24 IU/kg. At present, 2 of 10 patients reached the Hb value of 12 g/dl, which was the objective of this clinical trial, after 17 and 11 weeks of treatment, respectively. Their pretreatment values were 5.3 and 9.0 g/dl. One normotensive patient with a prior history of convulsions presented with a hitherto unexplained seizure episode and a transient hypertensive crisis when his Hb level reached only 10.3 g/dl. He then received 96 IU/kg of rHuEpo thrice weekly. In conclusion, thrice weekly administration of rHuEpo appears to be an efficient treatment allowing to obtain an improvement or even correction of anemia in chronic hemodialysis patients. Particular caution should be devoted to patients with a prior history of convulsions. The possibility of a resistance to rHuEpo in a subset of dialysis patients should be given further consideration.

Piridoxilate–induced oxalate nephropathy: A new variety of nephrocalcinosis. *Ph. Vigeral, S. Kenouch, D. Chauveau, B. Mougenot and J. Ph. Méry, (Service de Néphrologie, Hôpital Bichat and Laboratoire d'Anatomie et de Cytologie Pathologiques. Hôpital Tenon, Paris).* Several cases of calcium oxalate nephrolithiasis presumably due to hyperoxaluria have been recently reported in patients chronically treated with piridoxilate (P), a combination of glyoxylic acid and piridoxine. One of the metabolic pathways of glyoxylic acid is indeed oxidation into oxalic acid. It seems that oxalate nephropathy with renal insufficiency may also be induced by chronic (P) administration. This 70-year–old man had been taking (P) 450 mg daily since 1976 because of coronary disease. In April, 1985, serum creatinine was 168 μmol/liter. In June, 1985, a radio–opaque stone was demonstrated in the right inferior calix. Shock–wave lithotripsy was then performed and was followed by elimination of small fragments of stones made of whewellite. In October 1985, when the patient was still taking (P), daily urinary elimination of oxalate was 522 μmol (N < 330 μmol) and an early morning urine sample contained numerous crystals that infrared spectrometry showed to be whewellite. Serum creatinine was 329 μmol/liter. Renal biopsy showed chronic tubulo-interstitial nephritis with numerous intraluminal and intracellular crystals in the tubules which were birefringent when viewed under polarized light. (P) was then withdrawn. One month later, oxaluria was 110 μmol/day and crystalluria had disappeared. Serum creatinine was 334 μmol/liter. In conclusion, this observation shows that long–term treatment with (P) induces hyperoxaluria which in turn may result in calcium oxalate nephrolithiasis and chronic oxalate nephropathy.

Massive removal of antidiuretic hormone from plasma during hemofiltration stimulates its secretion in humans. *B. Viron, W. Pruszczynski, F. Mignon, R. Ardaillou, INSERM 64, Hôpital Tenon, Paris, France.* Antidiuretic hormone (ADH) was measured in the plasma and its ultrafiltrate in 11 patients with end–stage renal failure. The patients were hemodialyzed in order to obtain a state of normal hydration. Then high–rate hemofiltration was started using a polyacrylonitrile membrane. Nineteen liter of ultrafiltrate were produced in 170 minutes and continuously replaced by an isoosmotic substitution fluid to maintain constant weight. ADH concentration was not significantly different in the plasma (7.1 ± 0.4 and 7.4 ± 0.6 pg/ml before and after hemofiltration) and in the ultrafiltrate (6.6 ± 0.5 pg/ml). It did not change during the session and the following 24 hours. Total extracted ADH calculated from either ADH present in the ultrafiltrate or the difference between ADH entering and leaving the ultrafiltration system was 131 ± 10 ng. The corresponding ADH clearance was 114 ± 2.6 ml/min, which represented more than two–thirds of the metabolic clearance rate of the hormone as predicted from previous results obtained in this laboratory. Plasma osmolality, body weight, blood pressure and plasma renin activity were not modified during hemofiltration. These results demonstrate that ADH is freely filtered through the membrane studied and thus does not bind to plasma proteins. Furthermore, they indicate that ADH secretion is adequately stimulated in order to maintain plasma levels constant despite the increase in the metabolic clearance rate. We advance the hypothesis that ADH secretion increases rapidly in response to hemofiltration–induced ADH removal through a negative feed–back mechanism.

Culture and characterization of arteriolar smooth muscle cells from the rabbit renal cortex. *J. C. Dussaule, J. Perez, D. Chansel, R. Ardaillou, INSERM 64, Hôpital Tenon, Paris, France.* Cell cultures were performed from collagenase–digested renal cortex of rabbits after purification of an arteriole–rich fraction by successive sievings. Under the conditions of culture used (10% CO_2 atmosphere), smooth muscle cells rapidly grew whereas the other cell lines disappeared. A homogeneous culture of these cells was obtained through successive passages (2–6). They were identified as smooth muscle cells from their spindle–shape morphology and the presence of myofibrils with dense bodies under electron microscopy and also from their content in creatine kinase (1612 ± 771 mIU/mg protein; $N = 18$) which was 60 times higher than that of the initial cortical homogenate. These smooth muscle cells of arteriolar origin synthesized PGI_2 (6.7 ± 3.9 ng/mg/24 hr) and PGE_2 (14.5 ± 8.2 ng/mg/24 hr; $N = 8$). They exhibited β-adrenergic receptors as demonstrated by the stimulatory effect of isoproterenol on their cyclic AMP content (437 ± 124 and 34.7 ± 8.7pmol/mg with and without 200 μM isoproterenol, respectively). These cells also synthesized and released renin. Renin activity measured from angiotensin I formed in the presence of rabbit plasma devoid of renin was 5.9 ± 2.6 ng AI/hr/mg ($N = 24$) in the cell extracts. Active renin in the medium represented only 17% of that in the cells. This percentage reached 76% after acidification, which indicates that inactive renin was secreted for the most part. Specificity of renin activity assay was demonstrated by the high inhibitory effect of SR 42128, a specific blocker of the enzyme. Culture of smooth muscle cells from the renal cortical arterioles represents a new tool for the study of the synthetic functions and the receptors of these cells and thus for a better knowledge of the cortical circulation.

Antigenicity of glomerular basement membrane (BGM) in hereditary nephritis. *C. S. O. Savage, L. H. Noel, M. C. Gubler, R. Charbonneau, J. P. Grunfeld, C. M. Lockwood, Royal Postgraduate Medical School, Hammersmith Hospital London, U.K., Hôpital Necker, Paris, France.* In 20 of 42 patients with hereditary progressive glomerulonephritis (NH), absence of or reduced binding was observed on immunofluorescence immunoperoxidase staining of renal tissue, with those antibodies directed towards the Goodpasture autoantigen, namely human anti-glomerular basement membrane (GBM) autoantibodies (HuAb) and a monoclonal anti-human GBM antibody (MCA-P1). HuAb and MCA-P1 recognize the same 6 bands (between 22 and 54 Kd) in collagenase solubilized GBM (CS-GBM) following Western blotting. The antigenicity of the GBM in HN has been investigated further using collagenase digests of kidney from 3 patients with NH (CS-HNK) or 3 control end–stage kidneys (CS-ESK) and autoantibody containing sera (HNAb) from 4 patients with HN who developed anti-GBM nephritis following transplantation. In Western blotting studies, HuAb (6) and MCA-P1 showed the same binding patterns to CS-GBM and CS-ESK. However these reagents showed a different staining pattern on CS-HNK with absence of 3 of the 6 bands, comprising bands of 26, 30 and 54 Kd. The binding of the 4 NHAb to CS-GBM were dissimilar. Three showed identical binding to that seen with HaAb and MCA-P1 (to the 6 bands between 22 and 54 Kd), the fourth binds only to bands 26, 30 and 54 Kd, suggesting either heterogeneity in the HN Ab response to allografted kidneys or that a difference exists in the GBM determinants present in some patients with Alport's syndrome, a difference which may underline the clinical heterogeneity of the disease. Thus, our results show a relative rather an absolute loss of Goodpasture antigenicity within GBM of HN kidneys and imply that at least some of the gene encoding the Goodpasture antigen are probably normal. It is suggested that an abnormality resides in a gene which either encodes an enzyme responsible for linking the antigenic moiety of one set of antigen–carrying determinants or encodes that part of a subset of parent molecules to which the Goodpasture antigenic determinant normally binds.

Membranous glomerulonephritis after diclofenac treatment. *F. Schillinger, R. Montagnac, T. Milcent, Service de Néphrologie Hémodialyse, CHG Troyes, France.* Among drugs inducing nephrotic syndrome (NS), nonsteroidal anti-inflammatory drugs (NSAID) are

preponderant. They often induce the development of a minimal change glomerulopathy with or without associated interstitial nephritis, but only rarely cause membranous glomerulonephritis. We report a case of reversible membranous glomerulonephritis due to diclofenac administration. A 75-year–old man had been treated with diclofenac, 100 mg daily, for 45 days, because he suffered from degenerative joint disease of the knees. He presented with NS (7 kg wt increase) hypertension (170/100 mm Hg) and mild renal failure (serum creatinine 145 μmol/liter, creatinine clearance 60 ml/min). Immunological and etiological results were negative and histological examination revealed membranous glomerulonephritis. Diclofenac treatment had been discontinued immediately after admission; diuretics induced edema regression and NS remitted in 7 months, without corticosteroid or immunosuppressive therapy. NSAID related membranous glomerulonephritis has been reported in only 3 other cases; twice with diclofenac, once with ketoprofen. On the other hand, association of NS and acute renal failure, with minimal glomerular changes and severe tubulointerstitial lesions, is more and more often recognized during NSAID therapy. Isolated NS with minimal glomerular changes and without interstitial nephritis are also known. These side effects of NSAID, of late appearance in comparison with those due to inhibition of prostaglandin–mediated vasodilatation, seem to be immunologically mediated and present individual susceptibilities related to genetic factors. Indeed, the two other cases of diclofenac–related membranous glomerulonephritis in the literature developed in patients with rheumatoid arthritis, an immunological condition known to favor circulating immune complex formation in the presence of excess drug antigens.

IgE antibodies to isocyanates in dialysis patients. *F. Lavaud, S. Lavaud, O. Toupance, A. Berthier, J. Chanard, Centre Hospitalier et Universitaire, Reims, France.* Isocyanates which are chemicals used in the dialyzer–manufacturing process are well–known inducers of asthma in occupationaly exposed workers. However, allergy to isocyanates resulting from blood exposure has not been reported. Sensitization to these molecules was investigated in chronically hemodialyzed patients. Two groups were selected: group I, 9 patients having reactions characteristic of immediate–type hypersensitivity when starting dialysis; group II, 67 dialyzed patients without anaphylactic reactions. Eleven patients in this group had a history of atopy. IgE antibodies to isocyanates were detected using radioallergosorbent tests (RAST) for toluene diisocyanate, diphenylmethane diisocyanate, hexamethylene diisocyanate and by in vitro degranulation of purified human basophils (HBDT). In addition, sensitization to formaldehyde and ethylene oxide was investigated. In symptomatic patients IgE antibodies to isocyanates were detected at a significant level in 4 of 9 (44%) patients with RAST and in 9 of 9 with HBDT (100%). In patients without anaphylactic reactions only 7 (9%) and 9 (13%) patients had specific antibodies to isocyanates detected with RAST and HBDT, respectively. Sensitization to formaldehyde was detected in 1 patient of group I and in 2 patients of group II. Sensitization to ethylene oxide was detected in 2 patients of group I and in 3 patients of group II. Data show the widespread sensitization to isocyanates in patients exposed to hemodialysis, especially in patients with anaphylactic reactions where neither formaldehyde nor ethylene oxide can be implicated. Further studies are required to assess the specificity and the sensitivity of the tests in uremia.

Duration of protective effect of hepatitis B vaccine in staff and patients of dialysis centers: Determination of the optimal time for revaccination. *P. Jungers, A. M. Couroucé, A. Laplanche, E. Benhamou, F. Tron, Department of Nephrology, Necker Hospital and Centre National de Transfusion Sanguine, Paris, and Department of Medical Statistics, Institut Gustave Roussy, Villejuif and Direction des Recherches Cliniques Pasteur–Vaccins, Marnes la Coquette, France.* In an attempt to define the best revaccination strategy, we analyzed the long–term course of anti-HBs antibody (Ab) titers in medical staff and hemodialysis patients of French dialysis units protected with HEVAC B (Pasteur) vaccine. Of the 184 healthy staff members who participated in a multicenter efficacy trial (*Lancet* i:455, 1981), 143 received a first booster injection (B1) 15 months after 3 initial subcutaneous injections of 5 μg and were followed–up for 5 years. The mean (geometric) titer of Ab determined 1, 21, 43 and 60 months following B1 was 13,940, 1626, 592 and 492 mIU/ml, respectively. After 5 years, 93% of subjects still had a residual (protective) titer ≥ 10 mIU/ml, including 85% with titer ≥ 50 mIU/ml. The slope of Ab decline following B1 was biphasic, initially rapid (about 10-fold from 1 to 21 months) and then slower (about 3-fold from 21 to 60 months). All individual time–curves were parallel with a mean slope of − 0.108 Log/month from 1 to 21 months. Of the 215 hemodialysis patients who entered an immunogenicity trial (*Clin Nephrol* 21:143, 1984), 182 received a booster 14 months after the first injection and were followed–up for 2 years. Among those who received a reinforced protocol, Ab titer determined 1, 6, 12 and 24 months following B1 was 3282, 1142, 559 and 312 mIU/ml in group II (3 × 10 μg) and 2047, 914, 387 and 150 mIU/ml in group III (4 × 5 μg). After 2 years, 20% of groups II and III patients pooled together had a residual titer lower than 10 mIU/ml. Also, the slope of Ab decline was parallel in all subjects with a mean rate of − 0.107 Log/month and near 10-fold decline from 1 to 24 months. Time–curves of Ab decay for different levels of peak Ab titers are presented on diagrams allowing the individual determination of the residual Ab titer at any time following booster. In conclusion, in staff personnel and patients of dialysis units exposed to high risk of HBV infection and thus requiring sustained effective protection, titration of anti-HBs Ab level obtained after primovaccination is needed to assess protective efficacy and to evaluate the optimal time for revaccination.

The rate of progression of chronic renal failure in the various types of primary kidney diseases: A study of 167 cases. *P. Jungers, A. Ferhat, Ph. Chauveau, G. Albouze, T. Loubaris, T. Hannedouche, Department of Nephrology, Necker Hospital, Paris.* We retrospectively analyzed the spontaneous rate of progression of renal failure (RF) from an advanced stage, defined by plasma creatinine concentration (Pcr) of 500 μmol/liter towards maintenance hemodialysis (HD), in all patients suffering from primary chronic nephropathy with established diagnosis, having had at least 6 Pcr determinations throughout this time interval and receiving usual diet prescriptions. Among 625 patients who started HD at Necker Hospital from January 1981, to December 1985, 167 (93 males, 74 females) fulfilled these criteria and were analyzed. The primary nephropathy was chronic glomerulonephritis (CGN) in 55, chronic pyelonephritis (CPN) in 42, polycystic kidney disease (PKD) in 35, angionephrosclerosis (ANS) in 22, Alport's syndrome (AS) in 9 and non-insulin dependent diabetes nephropathy (DN) in 4. In all patients were recorded the time duration from Pcr 500 μmol/liter until HD (500-HD) and from Pcr 700 μmol/liter until HD (700-HD), and the mean slope of 1/Cr (expressed in μmol/liter × 100 per month). Mean (± 1 SEM) values observed in the different types of renal disease are shown in the table.

	No	500–HD	700–HD	1/Cr slope
CGN	55	14.3 ± 1.5	6.3 ± 0.8	−0.0157 ± 0.0019
CPN	42	19.4 ± 2.0	8.0 ± 1.1	−0.0087 ± 0.0012
PKD	35	17.2 ± 1.1	6.9 ± 0.9	−0.0064 ± 0.0005
ANS	22	11.6 ± 1.4	3.8 ± 0.5	−0.0133 ± 0.0026
AS	9	9.3 ± 1.5	4.3 ± 1.4	−0.0171 ± 0.0046
DN	4	9.2 ± 2.6	1.7 ± 0.5	−0.0362 ± 0.0183
Total	167	15.4 ± 0.8	6.3 ± 0.4	−0.0120 ± 0.0009

The mean values of 500-HD and 700-HD were significantly longer in CPN and PKD groups than in the CGN group, with the shorter courses being observed in ANS, AS and DN groups. The terminal rate of progression, expressed as the ratio 700-HD/500-HD, was accelerated in the ANS and DN groups (ratio < 0.40) when compared to the other groups (ratio ≥ 0.40). In conclusion, the spontaneous rate of progression of advanced chronic RF towards end–stage differs according to the type of the underlying renal disease. Our results provide epidemiologic baseline data for evaluating the possible effects of diet manipulation on the progression of RF in future trials.

Extrarenal epuration (E.R.E.) in salicylate intoxications. *R. Montagnac, F. Schillinger, T. Milcent, A. Dinh, B. Brones, CHG Troyes, France.* We hemodialyzed a 23-year–old patient for severe salicylate poisoning (ingestion of 40 g). He was comatos and presented with high blood salicylate level (1500 mg/liter) and hypoprothrom-

binemia (25.8%). We emphasize the advantages, in certain circumstances of severe salicylism, of E.R.E. which induces a decreased blood level and consequently much better prognosis. (1.) Deaths are still too frequent while E.R.E. is very efficient for intoxication by aspirin. Aspirin has a small molecular weight, diffuse mainly extracellularly and is slightly bound to proteins. (2.) When its intrinsic risks are considered, indications of E.R.E. are various, linked to absorption rate, blood salicylate level, acid–base disturbances, hypoprothrombinemia, central neurologic manifestations and eventual associated renal failure. (3.) Apart from hemofiltration, which has not been adequately assessed but is certainly interesting, we consider hemodialysis the better active treatment if material is available. Its efficiency is higher than peritoneal dialysis, even if both correct associated disturbances (hypothermia, acidosis, metabolic disorders) in contrast to hemoperfusion. The latter, although as efficient as hemodialysis, presents several of its own disadvantages that reserve it, for some authors, to poisoning with other drugs that are more dangerous and/or have a different pharmacology.